## REMARKS

Claims 1, 3-17 are pending and under consideration.

*Claim Rejection – 35 USC § 103*

Claims 1, 3-17 are rejected under 35 USC § 103, as being unpatentable over Eggeling et al. (Hum Genet., Vol 99, pages 266-270, 1997) ("Eggeling") in view of Ando et al. (J Clin Microbiol., Vol.35, No.3, pages 570-577, 1997) ("Ando").

The Office states that Eggeling teaches the claimed methods except for the use of a mixture of at least two DNA polymerases (Action p.3-4). The Office then states that Ando teaches a method for the amplification of nucleic acid fragments using a mixture of at least two DNA polymerases, at least one of which possesses 3'-5' exonuclease activity (Action p.4).

The Office asserts that Eggeling could be combined with Ando to render obvious the use of a mixture of DNA polymerases with the method of claims 1, 3-17 "to achieve the expected advantage of developing a high sensitive amplification of long templates of nucleic acid molecules" (Action p.5). Applicants respectfully traverse the rejection.

Applicants assert that the claimed invention is not directed to problems with the amplification of long templates of nucleic acid molecules. "The method provided by the invention is suitable for use in the amplification of nucleic acid fragments having a length between 100 and 1000 base pairs. The method is especially suited for use in the amplification of nucleic acid fragments having a length between 150 and 550 base pairs" (Specification p 7. lines 10-13). Ando describes methods to efficiently amplify a 3-kilobase region of nucleic acid. Applicants assert that it was well known in the art that amplification of a 3-kilobase region is different than amplification of a smaller region, <1000 base pairs. One skilled in the art would not have been motivated to use a mixture of DNA polymerases in the second specific amplification step because such mixtures were only used in the art in the amplification of long templates. Applicants assert that the Office has not provided the motivation for an ordinary practitioner to combine the teachings of Ando with Eggeling. Accordingly, the combination of the two references does not render claims 1, 3-17 obvious. Applicants respectfully request withdrawal of the rejection.

Additionally, Applicants assert that the claimed invention provides surprising improvements to the preamplification methods known in the prior art. "The use of

polymerase mixtures in the primer-extension preamplification PCR provided by this invention leads to a surprisingly high sensitivity of DNA detection that cannot be achieved using the methods known from the prior art" (Specification p.6 lines 27-29). Applicants assert that these surprising results show that the use of a mixture of at least two DNA polymerases (Ando) was not obviously combined with preamplification methods (Eggeling) known in the art, and there is no suggestion provided in either Ando or Eggeling to combine these two references. Accordingly, the combination of the two references does not render claims 1, 3-17 obvious. Applicants respectfully request withdrawal of the rejection.

## CONCLUSION

Applicants respectfully assert that the present application is in condition for allowance and request that the Office issue a timely Notice of Allowance. A petition for a 1 month extension of time is being filed concurrently with this Response. Please grant any other extensions of time required to enter this amendment and charge any additional fees or credit any overpayments to Deposit Account No. 50-0812.

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